A Clinical Study on Malignant Pleural Effusion

Zay Soe [1]*, Zaw Aung [2], Khin Darli Tun [3]

[1] Dr Zay Soe- MB, BS. M Med Sc (Int Med). DTCD (Wales). Dr Med Sc (Respiratory Medicine). DTM&H (London), FACTM. FCCP (USA). Email zaysoe13@gmail.com. Associate Professor and Head of the Internal Medicine Department, UCSI University, Malaysia
[2] Senior Lecturer, Department of Internal Medicine, School of Medicine, UCSI University, Malaysia.
[3] Senior Lecturer, School of Medicine, UCSI University, Malaysia.

Corresponding Author: Zay Soe- MB, BS. M Med Sc (Int Med). DTCD (Wales). Dr Med Sc (Respiratory Medicine). DTM&H (London), FACTM. FCCP (USA). Email zaysoe13@gmail.com. Associate Professor and Head of the Internal Medicine Department, UCSI University, Malaysia

ABSTRACT

INTRODUCTION
Malignant pleural effusion (MPE) is one of the commonest causes of pleural effusion in Myanmar. The diagnosis of MPE can be sometimes difficult to make because of the inconclusive result of pleural biopsy report. We studied the clinical features of MPEs as well as diagnostic procedures.

OBJECTIVE
Our research goal and the objective of the study are to review the natural history of patients with a malignant pleural effusion but without obvious evidence of a primary lesion and to assess the value of diagnostic investigations to confirm the malignant pleural effusion. To follow the objectives, we collect the information on the disease characteristics such as age, gender, clinical features, nature and microscopic examination of pleural fluid, positivity rate of blind pleural biopsy results in patients diagnosed with bronchogenic carcinoma in the Chest Medical Department in Yangon General Hospital, Myanmar.

METHODS
This study was a hospital based descriptive cross sectional study, performed at Chest Medical Department, Yangon General Hospital, Myanmar, from January 2004 through January 2005. Thorough history taking and physical examinations, radiological findings, hematological and serum biochemical profiles were recorded. Pleural aspiration and biopsy were also performed.

RESULTS
43 males and 30 females presenting with malignant pleural effusion were included in this study. The commonest age group lies between 61 to 70 years old with mean ± SD age of 63.45. 60 patients (82.2%) of malignant pleural effusions are heavy smokers or ex-smokers. 65 patients (88.9%) were diagnosed by identification of malignant pleural tissue in blind pleural biopsy, 8 patients (11.1%) were diagnosed by identification of malignant cells in the pleural fluid

cytology because biopsies revealed chronic nonspecific pleuritis. Among histologically identified cell types most patients (33) had metastatic large cell carcinoma. Pleural fluid cytology for malignant cells was positive in 47 patients (64.4%). Common symptoms of malignant pleural effusions were breathlessness, cough, chest pain, weight loss and loss of appetite. Common physical signs were cachexia, fever on admission, palpable lymph node. Clinical features of consolidation and collapse were also noted in chest examinations. 45 patients had left sided effusion (61.6%) and 28 had right sided (38.4%). 47.9 % of pleural aspirate were blood stained. Mean ADA activity (SD) in malignant pleural effusion was 23.83 U/L. Mean protein concentration was 41.02 g/l, mean pleural fluid serum protein ratio was 0.61, LDH was 599.56 U/L, mean pleural fluid / serum LDH ratio was 1.18. Mean total and differential white cell counts of peripheral blood were within normal limits. Mean ESR was 62.23.

CONCLUSION
Pleural fluid biochemical analysis can have an important contribution for investigation of patients with pleural effusion. The Light's criteria is fulfilled in all cases of MPEs. Repeated pleural biopsy procedures will be necessary if first session failed to fetch the definitive tissue diagnosis. Pleuroscopy is recommended procedure for tissue diagnosis in MPEs.

Keywords: Malignant pleural effusion (MPE), pleural biopsy, Light's criteria, Pleural fluid chemical analysis.

Introduction

Malignant pleural effusions (MPEs) are a troublesome and debilitating complication of advanced malignancies. MPEs are one of the commonest causes of pleural effusion in Myanmar. According to the hospital statistics, approximately 500 patients with various causes of exudative pleural effusion were admitted to Chest Medical Ward, Yangon General Hospital in every year. The commonest causes are tuberculosis and malignant pleural effusions.

Malignant pleural effusions are most commonly associated with cancer of the breast, lung, gastrointestinal tract, ovary, and with lymphomas.Malignant effusions also occur with pleural metastases, direct extension of lung cancer to the pleura, impaired lymphatic drainage from mediastinal tumors without direct pleural invasion (particularly in lymphoma).
The mechanisms that cause the effusions include increased capillary permeability that allows fluid leakage into the pleural space, decreased oncotic pressure that normally holds fluid in the intravascular space due to hypoalbuminemia, increased negative pressure in the pleural space as a result of atelectasis.[1]

A pleural effusion is a condition where abnormal fluid builds up in the pleural space. The accumulation of pleural fluid can usually be explained by increased pleural fluid formation or

decreased pleural fluid absorption, or both. Increased pleural fluid formation can result from elevation of hydrostatic pressure, decreased colloid osmotic, increased capillary permeability, passage of fluid through openings in the diaphragm, or reduction of pleural space pressures. Decreased pleural fluid absorption can result from lymphatic obstruction or from elevation of systemic venous pressures resulting in impaired lymphatic drainage (e.g., superior vena cava obstruction syndrome). In patients with MPE, metastasis to pleural spaces may causes significant shifts or fluid imbalance from derangements in the Sterling forces that regulate the reabsorption of pleural fluid [2]. That derangement may cause MPE.

MPE is caused by cancer that grows in the pleural space. It can be a complication of virtually any malignancy. The pleura is involved in neoplastic disease more commonly through metastasis than through primary tumours. Lung and breast cancers are the leading causes of metastatic disease to the pleura. Other less common causes are hematologic (e.g., lymphoma, leukemia), ovarian, mesothelioma and gastrointestinal tumours. Cytological examination of the pleural fluid is positive in more than 50% of cases with pleural involvement.

Primary and metastatic pleural neoplasms, and non-neoplastic pleural diseases, can have similar clinical, radiographic and gross features. However, treatments and prognoses of these diverse pleural conditions vary greatly. Accurate diagnosis of pleural disease is therefore extremely important, and histological interpretation of pleural biopsies is vital to rendering an accurate diagnosis. Smaller biopsies contribute to the difficulties in accurately characterizing pleural lesions, and immunostains are frequently employed in their assessment.[3]

Malignant pleural effusion is a common and debilitating complication of advanced malignant diseases. This problem seems to affect particularly those with lung and breast cancer, contributing to the poor quality of life. Approximately half of all patients with metastatic cancer develop a malignant pleural effusion at some point, which is likely to cause significant symptoms such as dyspnea and cough. Evacuation of the pleural fluid and prevention of its re-accumulation are the main goals of management.[4]

Tumor markers (e.g., carcinoembryonic antigen) are not specific enough to be recommended routinely in establishing the diagnosis. Immunocytometry has been used to establish the diagnosis of lymphoma and has been helpful in cases of idiopathic effusions when conventional techniques were non-diagnostic. [5]

Quality of life with MPE is often compromised due to debilitating symptoms like shortness of breath, dry cough, pain, feeling of chest heaviness, inability to exercise and malaise (feeling unwell)

The diagnosis of malignant pleural effusion as well as finding of the exact location of the pleural effusion, or plan treatment will be based on physical examination, chest x-ray, Computed tomography scan, ultrasound and thoracentesis.

The presence of fluid in the normally negative-pressure environment of the pleural space has a number of consequences for respiratory physiology. Pleural effusions produce a restrictive ventilatory defect and also decrease the total lung capacity, functional residual capacity, and forced vital capacity. [6] They can cause ventilation-perfusion mismatches and, when large enough, compromise cardiac output.

Evaluation of exudative pleural effusion usually includes thorough history, complete clinical examination, appropriate blood tests, radiographs, studies of pleural fluid and needle biopsy of

pleura using Abram's pleural biopsy needle or Cope's biopsy needle. However following these procedures some patients still have undiagnosed condition and the clinical management of these cases is controversial. The initial step of the investigation is the distinction between transudates and exudates, as this gives an indication of the pathophysiologic mechanisms, the differential diagnosis and the need for further investigations.

Various tests can be done on pleural fluid to determine the cause of a pleural effusion. If a malignant effusion is suspected, the fluid will be sent for cytology analysis. About 50% to 60% of cytology tests on pleural fluid are positive for malignancy in patients already known to have cancer. At least 250 mL of pleural fluid is needed for a proper cytologic examination. Other tests done on pleural fluid include protein, LDH, glucose, pH, and cell counts. If a patient has cancer, but the pleural cytology is negative and there is no other obvious cause of the effusion (as will occur in about 25% of cases), thoracoscopy can be performed to confirm the diagnosis through a pleural biopsy of abnormal areas of the pleurae under direct visualization. Thoracoscopy is diagnostic in at least 90% of patients with malignant pleural effusion.[1]

In a randomized controlled trial, Abrams' biopsy correctly diagnosed malignancy in eight of 17 patients (sensitivity 47%, specificity 100%, negative predictive value 44%, positive predictive value 100%).[7]

Because of their high sensitivity in identifying exudates, the criteria proposed by Light et al[8] have become the standard method for making the distinction. The classic work of Light and colleagues demonstrated that 99% of pleural effusions could be classified into two general categories: transudative or exudative .A basic difference is that transudates, in general, reflect a systemic perturbation, whereas exudates usually signify underlying local (pleuropulmonary) disease. The 'Light' criteria include a pleural fluid to serum protein ratio greater than 0.5, a pleural fluid to serum LDH ratio greater than 0.6 and a pleural LDH concentration more than two thirds normal upper limit for serum. If any one of these critical values is exceeded, the effusion is exudates. The original study of Light and colleagues had a diagnostic sensitivity of 99% and specificity of 98% for an exudates.

In a study by Alemán C et al, 1014 consecutive pleural effusion patients were treated over a 12-year period, of whom 346 were diagnosed as having an idiopathic or malignant aetiology. Eighty-three patients with idiopathic effusions and 263 with malignant effusions were included. Idiopathic pleural effusion resolved in 47 patients, improved in 20 and persisted in 16. Biochemical pleural fluid analysis did not predict these outcomes. A history of neoplasm, chest X-ray and CT features, as well as additional examinations according to clinical findings, established a diagnosis or suspicion of malignancy in 256 (97.7%) of the 263 patients who received a diagnosis of malignant effusion. Diagnostic thoracoscopy was helpful in seven patients in whom malignant disease was strongly suspected, despite the absence of other pathological findings.[9]

In this study we report our experience with 73 patients with confirmed diagnosis of MPE and discuss the clinical features, radiological findings, biochemical, cytological and microbiological analysis of pleural fluid, hematological and biochemical profiles of serum and positivity rates of blind pleural biopsy in these patients. We also analyzed the likelihood ratios of some of the important presenting features in this study.

OBJECTIVES

The objective of the study was to review the natural history of patients with a malignant pleural effusion but without obvious evidence of a primary lesion and to assess the value of investigations to confirm the diagnosis of malignant pleural effusion. We would also like to report our experience of the disease characteristics such as age, gender, clinical features, nature and microscopic examination of pleural fluid, positivity rate of blind pleural biopsy results in patients diagnosed with bronchogenic carcinoma in the Chest Medical Department in Yangon General Hospital, Myanmar.

Material and Method

Patients

This study was a hospital based descriptive cross sectional study performed at the Department of Respiratory Medicine, Rangoon General Hospital (RGH), Myanmar from January 2004 through January 2005. We did not perform any sampling procedure. All patients with positive pleural tissue biopsy for malignancy or presence of malignant cells in pleural fluid were included except those with following exclusion criteria.

Exclusion criteria

1. Multiple pathology of pleural effusion

Patients with more than one etiology of pleural effusion were excluded.

2. Patient's refusal

Written informed consent was obtained from patient. Before requesting consent, the individual was explained in an understandable language about the aims of the study, the methods of conduct, expected duration of subject participation, benefits, foreseeable rights or discomfort, the extent of confidentiality, extent of investigators responsibility, provision of medical services, the right to refuse to participate and withdraw from the study without affecting further medical care.

Detailed history, thorough physical examination, radiological findings, haematological and biochemical findings were recorded in the proforma. Pleural aspiration and biopsy was performed on all patients after obtaining the written consent. Macroscopic findings, cytological, microbiological and biochemical analysis of pleural fluid were performed in all patients.

History taking

Symptoms such as the history of fever, cough, sputum, haemoptysis, dyspnoea, chest pain, weight loss, loss of appetite were recorded and analyzed. Detail history of smoking were recorded.

Physical examinations

Patient's general conditions such as cachexia, body weight, breathlessness, fever were noted. Physical signs such as cervical or scalene lymph node enlargement, clubbing, SVC obstruction were also recorded. Thorough respiratory system examination was done to find out features of collapse, consolidation and pleural effusion.

Radiological examinations
CXR (PA) view was taken in every patient and lateral view was taken, if necessary. The amount of fluid, the side involved, hilar and/or mediastinum lymphadenopathy, parenchymal involvement, cavitation and any other radiographic abnormalities were noted.

Serum haematological and biochemical profiles
Full blood count and ESR were done in every patient. Plasma total and differential protein and LDH were taken in every patient to calculate the ratio fulfilling 'light' criteria.

Pleural fluid aspiration

Macroscopic appearance of pleural fluid. Macroscopic appearance of pleural aspirates was recorded.

Cytology, cell types and cell counts. Differential white cell counts of pleural fluid were recorded and calculated as percentage. The actual number of cells was not counted.

Biochemistry of pleural fluid. Determination of pleural fluid total protein concentration (g/l), LDH(U/L), total cholesterol (mmol/l) and sugar (mmol/l) were performed . To differentiate transudate from exudate, the ratio of pleural fluid and serum protein ; the ratio of pleural fluid and serum LDH were calculated. Pleural fluid Adenosine deaminase level was measures by Giusti and Galanti method.

Pleural biopsy
All patients were subjected to thoracentesis and closed pleural biopsy using Abram's needle (Figure 1) after obtaining a written consent. It is a blind procedure and if no definite tissue diagnosis was obtained after 3rd session, the patient was classified as undiagnosed and excluded from the study unless pleural fluid cytology for malignant cells was detected.

Statistical Analysis
All the background clinical data were recorded in standardized proforma. Record files were constructed in the Microsoft Excel software. The final data file in the form of record file in Microsoft Excel was exported as data base file and it was opened in the SPSS 16.0 for Windows software. Descriptive statistics including mean with SD, median, minimum and maximum values were calculated. Correlations of regression Coefficients (finding of r value) and P- value were calculated among pleural fluid biochemical finding were tabulated. The correlation matrix of multiple regressions among independent variables of pleural was created as multiple small scattered diagrams with regression line. Likelihood ratios of some of the clinical features were also calculated.

Results

Patients with malignant effusions included 43 males and 30 females. (Figure 2)

The commonest age group of malignant pleural effusion lies between 61 to 70 years old. Out of 73, 63 patients were above the age of 50. The mean ± SD age of 63.45 ± 10.5 (youngest was 38 years old and oldest was 85 years). (Figure3)

60 patients (82.2%) of malignant pleural effusions are heavy smokers or ex heavy smokers.

Common symptoms of malignant pleural effusions were breathlessness (86.3%),cough (86.3%), chest pain (72.6%), weight loss (68.5%), loss of appetite (76.7%) and sputum production (53.4%) and fever (41.1%). 15 patients (20.5%) has history of haemoptysis before admission (Figure 4).

Common physical signs were cachexia (49.3%), Fever on admission (37.0%) palpable lymph node (37.0%) clubbing (28.8%) and svc obstruction (11%) were recorded. Clinical signs of consolidation and collapse were noted 11.0% and 16.4% respectively besides signs of pleural effusion. (Figure 5)

The likelihood ratios (LR) of some of the possible associate features were calculated. The presence of chest pain (positive likelihood ratio LR 3.6) and consolidation (positive likelihood ratio LR 4.7) for hemoptysis were noted. The likelihood ratio of SVC obstruction for pulmonary collapse was negative LR 1.02. The likelihood ratios of other possible associate features were also calculated and revealed negatives.

45 patients had left sided effusion (61.6%) and 28 had right sided (38.4%) (Table1). No one presented with bilateral malignant pleural effusion in this study.

Table (2) shows pleural fluid macroscopic appearance of 73 malignant effusions. Out of 73, 35 had blood stained (47.9%) and the rest had straw colour aspirates (52.1%).

Mean ADA activity (SD) in malignant pleural effusion was 23.83 (13.64) U/L (minimum 1.0 . maximum 56.0). Regarding the biochemical profiles of malignant pleural effusions, mean protein concentration was 41.02 g/l, mean pleural fluid serum protein ratio was 0.61 ± .12, LDH was 599.56 U/L, mean pleural fluid / serum LDH ratio was 1.18 ± 0.51 U/L. Mean glucose and cholesterol of malignant PE were 4.78 ± 1.9 mmol/l and 2.31 ± 0.59 mmol/l respectively. Mean haemoglobin concentration was 10.8 ± 1.65 g/dl. Mean total and differential white cell counts of peripheral blood were within normal limits. Mean ESR was 62.23. (Table3)

In Table (4), calculation of correlation coefficient had also been analysed among parameters of pleural fluid as well as peripheral blood WBC subsets. Pleural fluid biochemical parameters mentioned in this table is also presented as correlation matrix in figure (6). In this figure, linear correlation is noted between pleural fluid protein and serum protein, pleural fluid protein and pleural and serum LDH ratio, pleural fluid protein and pleural fluid cholesterol, pleural fluid LDH and pleural fluid cholesterol, pleural and serum protein ratio and pleural fluid LDH. There are no associations among other biochemical profiles of MPEs.

Out of 73 malignant effusions, 65 patients (88.9%) were diagnosed by identification of malignant pleural tissue. 8 patients (11.1%) were diagnosed by identification of malignant cells in the pleural fluid cytology because subsequent biopsies revealed chronic non specific pleuritis (Table 5). They were diagnosed by pleural fluid cytology and exact histological type of malignancy may not be identified in the cytology report.

Pleural fluid cytology for malignant cells was positive in 47 patients (64.4%) and rest were negative (Table 6).

Among histological identified cell types, most patients (33) had metastatic large cell carcinoma, The rest were 11 patients with small cell type, 11 patients with adenocarcinoma and 10 patients with squamous cell carcinoma (Figure 7).

Discussion

MPEs were more common in male than female. It may be related to chronic smoking history in male patient. It is obvious that incidence of MPEs is significantly higher in patients with age above 50 and those with history of heavy smoking. 82.2% of malignant pleural effusions are heavy smokers or ex heavy smokers. Heavy smoking is the primary cause of the high prevalence of this disease.

Dyspnea and cough were significant symptoms in one study [4]which is consistent with our finding. In our study, breathlessness, cough, chest pain, weight loss, loss of appetite, and sputum production are common symptoms of malignant pleural effusion. Less than 50% of patient developed fever. Haemoptysis is an uncommon symptom of MPE (20.5%).

According to the likelihood ratio calculation, chest pain and pulmonary consolidation are the important features for haemoptysis. These signs should guide in clinical teaching. Other features are not positively associated to each other in likelihood ratio calculation. MPEs were more common on left side and the reason of side predilection is unknown.
Half of the pleural aspirates of MPEs were blood stained in their morphologic appearances.
Mean ADA activity (SD) in malignant pleural effusion was general low. In our previous report, mean ADA activity of TB pleural effusion was significantly higher than malignant group (73.91 Vs 23.83)[10].
There was a linear correlation among biochemical parameters of pleural fluid such as protein, LDH, and cholesterol. This can be concluded that production of all biochemical parameters in abnormal pleural fluid are related to single aetiology probably by inflammatory process. It is also suggested that pleural fluid levels of protein and LDH are partially depends on their plasma values and need measuring the plasma levels at the same time to get more accurate result. M Keshmir stated that pleural fluid cholesterol can be used to differentiate tuberculous from malignant pleural effusion[11]. There was no association between MPEs and any WBC subsets of peripheral blood.
Although a number of tests have been proposed to differentiate pleural fluid transudates from exudates, the tests first proposed by Light et al have become the criterion standards [8]. The fluid is considered exudates if any of the following apply:
Ratio of pleural fluid to serum protein greater than 0.5
Ratio of pleural fluid to serum lactate dehydrogenase (LDH) greater than 0.6
Pleural fluid LDH greater than two thirds of the upper limits of normal serum value
In our study, the nature of MPE was that of an exudates which is easily demonstrable by measuring protein and LDH in serum and pleural fluid, applying the Light criteria.
Light RW et al also found that pleural fluid glucose level below 60 mg/dl (3.3 mmol.l) suggests MPE, TPE or lupus pleuritis. In our study mean pleural fluid glucose concentration was 4.8 mmol/l which is not consistent with the finding of Light et al.
Most of the patients with MPE were anaemic (Mean haemoglobin concentration was 10.8 ± 1.65 g/dl) which are considered as multiple aetiology such as anaemia of chronic disease, depression, lack of nutrition and dietary deficiency. No leukocytosis is noted. Mean ESR was high at 62.23 which reflects inflammatory state in general. It has no diagnostic value for any specific disease.

Diagnostic pleural aspiration and pleural biopsy could be performed by a single session of procedure. Since it is a blind procedure and in patients with non-informative pleural fluid and pleural biopsy examinations, the procedure needed to be repeated.

Cagle PT, Allen TC pointed out that smaller biopsies contribute to the difficulties in accurately characterizing pleural lesions, and immunostains are frequently employed in their assessment.[3] But in our study, we could not perform special staining procedures of the histology slides because of limited facilities.

The positivity rate of first session of pleural biopsy was 65.7 % of MPE in this study. The second and third biopsy sessions were needed for the rest of patients. Repeat performance of pleural biopsy is obviously an inconvenience to the patients and also consumes a certain amount of medical resources. Closed pleural biopsy is a fairly blind procedure rendering it into a diagnostic procedure with less than desired positivity rate. Pleuroscopy resolves the diagnostic problem but the procedure requires more material resources and expertise.

. 8 patients (11.1%) were diagnosed only by identification of malignant cells in the pleural fluid cytology because subsequent biopsies revealed chronic nonspecific pleuritis. They were diagnosed by pleural fluid cytology and exact histological type of malignancy may not be identified in the cytology report. However, 64.4% of overall MPEs revealed positive pleural fluid cytology for malignant cells which is a substantial number to diagnosed MPEs even though exact histology cell type is difficult to identify. This finding supports that statement about 50% to 60% of cytology tests on pleural fluid are positive for malignancy in patients already known to have cancer[1].

In a randomized controlled trial, Abrams' biopsy correctly diagnosed malignancy in eight of 17 patients (sensitivity 47%, specificity 100%, negative predictive value 44%, positive predictive value 100%).[7] In our study, 88.9% of patients were correctly diagnosed malignancy but needed to be repeated in 23.2%.

In our study, metastatic large cell carcinoma was the commonest histologically identified cell type. The origin is considered from bronchogenic carcinoma.

References

1. Malignant Pleural effusion:Atrium Clinical Update Web site. Available at www.atriummed.com. Accessed December 2002.

2. Joe B. Putnam Jr. Malignant pleural effusion. *Surg Clin N Am.* 2002:*82,* 867-883.

3. Cagle PT, Allen TC. Pathology of the pleura: what the pulmonologists need to know. *Respirology.* 2011 Apr;16(3):430-8. doi: 10.1111/j.1440-1843.2011.01957.x.

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4. Neragi-Miandoab S. Malignant pleural effusion, current and evolving approaches for its diagnosis and management. *Lung Cancer*. 2007 Feb;55(2):253-4.

5. Raed A Dweik. Immunocytometry and gene rearrangement analysis in the diagnosis of lymphoma in an idiopathic pleural effusion. *Am Rev Respir Dis*.1992: *145*: 209-211.

6. Chalhoub M, Cruz AA, Marcilio C, Netto MB (1985), Effects of pneumothorax or pleural effusion on pulmonary function. *Thorax.* 1985:40: pp 60-65.

7. Maskell NA, Gleeson FV, Davies RJ . Standard pleural biopsy versus CT-guided cutting-needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial. *Lancet.* 2003 Apr 19;361(9366):1326-30.

8. Light RW, MacGregor MI, Luchsinger PC (1972). Pleural effusions: The diagnostic separation of transudates and exudates. *Ann Interm Med* ,1972: 77,507.
9. Alemán C, Sanchez L, Alegre JQJM et al. Differentiating between malignant and idiopathic pleural effusions: the value of diagnostic procedures. *QJM.* 2007 Jun;100(6):351-9.
10. Zay Soe, Wana Hla Shwe, Soe Moe. Value of pleural fluid Adenosine deaminase in Tuberculosis, *International Journal Publication-International Journal of Collaborative Research on Internal Medicine and Public health(IJCRIMPH)* 2010:Vol.2, No.3, pages 32-48.
11. M Keshmir, Use of cholesterol to differentiate tuberculous from malignant pleural effusion. *Med J Iran Hosp*, 2006:Vol 3 No1 Pages 34-37
2. Muhammad Abdul Hadi, et al. Knowledge And Perception Of Breast Cancer Among Women Of Various Ethnic Groups In The State Of Penang, Malaysia: A Cross Sectional Survey. *Med Princ Pract*. 2010;19(1):61-7.

TABLES

Table 1: Side of chest involved in patients with malignant pleural effusion

Side	Frequency	Percent
Right side	45	61.6
Left side	28	38.4
Total	73	100.0

Table 2: Pleural fluid morphology of malignant pleural effusion

Pleural fluid morphology	Frequency	Percent
Blood stained fluid	35	47.9
Straw coloured fluid	38	52.1
Total	73	100.0

Table 3: Biochemical and haematological data of serum and pleural fluid of patients with malignant pleural effusion

VARIABLES (unit)	Valid No. of patients 'n'	Mean	Median	Minimum	Maximum	Standard deviaton
AGE (years)	73	63.4521	60.9988	65.9053	38.0000	85.000
BIOCHEMICAL LEVELS						
Pleural fluid ADA(U/L)	73	23.8315	20.6472	27.0158	1.0000	56.000
Pleural fluid (PF) Protein (g/L)	73	41.0274	38.9712	43.0836	23.0000	67.000
Serum (S) Protein (g/L)	73	66.8767	65.2607	68.4927	50.0000	81.000
(PF:S)Protein	73	.6146	.5864	.6428	.3521	.933
Pleural fluid(PF) LDH (U/L)	73	599.5616	543.0500	656.0733	138.0000	1147.000
Serum (S) LDH (U/L)	73	538.9452	494.8029	583.0875	271.0000	1513.000
(PF:S) LDH	73	1.1791	1.0583	1.2998	.3750	2.786
Pleural fluid Glucose (mMol/L)	73	4.7890	4.3305	5.2476	1.1000	10.400
Pleural fluid Cholesterol (mMol/L)	73	2.3055	2.1669	2.4441	1.1000	3.400
PLEURAL FLUID LEUCOCYTE SUBSETS (%Total wbc)						
Lymphocytes	73	85.1389	80.0424	90.2353	20.0000	100.000
Neutrophils	73	12.8194	7.6939	17.9450	0.0000	80.000
Histiocytes	73	2.1806	1.3885	2.9726	0.0000	22.000
PERIPHERAL BLOOD HAEMATOLOGICAL LEVELS						
Haemoglobin (Gm%)	73	10.8356	10.4505	11.2208	8.1000	16.500
Polymorphs (% Total wbc)	73	67.1507	65.4747	68.8267	54.0000	93.000
Lymphocytes (% Total wbc)	73	26.2055	24.7004	27.7105	5.0000	38.000
Monocytes (% Total wbc)	73	4.2192	3.6408	4.7976	0.0000	18.000
Eosinophils (% Total wbc)	73	2.0137	1.6919	2.3355	0.0000	7.000
Basophils (% Total wbc)	73	.4722	.2712	.6732	0.0000	4.000
ESR (mm/1st hour)	73	62.2329	55.7666	68.6992	15.0000	130.000

Table 4: Correlation between biochemical variables of malignant pleural effusion

VARIABLES	Pleural fluid (PF) Protein	Serum (S) Protein	PF:S Protein	Pleural fluid (PF) LDH	Serum (S) LDH	PF:S LDH	Pleural fluid (PF) Glucose	Pleural fluid (PF) Cholesterol	Pleural fluid (PF) Lympho	Pleural fluid (PF) Neutrophil
Age	-.051187	.052612	-.062814	.046492	.195381	-.101152	.192279	-.203994	-.082401	.099720
Pleural fluid (PF) Protein	1.000000	.416136	.881486	.188268	.016205	.211654	.194264	.233965	.032308	-.070220
Serum (S) Protein	.416136	1.000000	-.052607	-.144864	.017628	-.097150	.147921	-.116685	-.022085	.007101
PF:S Protein	.881486	-.052607	1.000000	.286184	.014102	.279447	.126467	.312724	.036410	-.072397
Pleural fluid (PF) LDH	.188268	-.144864	.286184	1.000000	.198673	.759173	-.045869	.217216	.043571	-.022244
Serum (S) LDH	.016205	.017628	.014102	.198673	1.000000	-.382342	.083938	-.153335	-.054427	.046867
PF:S LDH	.211654	-.097150	.279447	.759173	-.382342	1.000000	-.080585	.273275	.107472	-.097633
Pleural fluid -Glucose	.194264	.147921	.126467	-.045869	.083938	-.080585	1.000000	-.035785	.179721	-.211816
Pleural fluid -Cholesterol	.233965	-.116685	.312724	.217216	-.153335	.273275	-.035785	1.000000	.035062	-.047586
Pleural fluid - Lymphocyte	.032308	-.022085	.036410	.043571	-.054427	.107472	.179721	.035062	1.000000	-.986983
Pleural fluid -Neutrophil	-.070220	.007101	-.072397	-.022244	.046867	-.097633	-.211816	-.047586	-.986983	1.000000
Pleural fluid ADA	.079306	-.031338	.089280	-.043783	-.157020	.061718	.191546	-.147568	-.024046	.040455
Peripheral blood										
Polymorphs	-.199370	-.015562	-.202607	-.187662	.095665	-.194357	.039386	.054934	.054162	-.041657
Lymphocytes	.189966	-.059608	.236394	.172040	-.130994	.220847	.140083	-.219225	-.076794	.060991
Monocytes	.113835	.213069	.004547	.088678	.090354	-.021604	-.202245	.329337	.087773	-.088052
Eosinophils	.013254	-.186909	.110146	.112865	-.071054	.173311	.121923	-.192271	-.055960	.063275
Basophils	.058921	.112272	-.004411	-.098629	-.098810	-.029875	-.087563	-.111051	.027100	-.022678
ESR	.150205	.076974	.139309	.002161	-.255910	.147919	.181896	-.058287	-.050963	.034246

Table 5: Percentage positivity of pleural biopsy in patients with malignant pleural effusion

Diagnostic positivity of pleural biopsy to obtain definite tissue diagnosis	Number of patients (%)
1st biopsy	48 (65.7 %)
2nd biopsy	14 (19.1 %)
3rd biopsy	3 (4.1 %)
Negative Biopsy but positive pleural fluid cytology of malignant cells	8 (11.1 %)
Total	73

Table 6: Pleural fluid cytology for malignant cells

Report	Frequency	Percent
Positive	47	64.4
Negative	26	35.6
Total	73	100.0

FIGURES

Figure (1). Abram's pleural biopsy needle

Figure (2). Sex distribution among patients with malignant pleural effusions.

Figure (3). Histogram showing distribution of patients' age group in malignant pleural effusion

Figure (4). Percentage of presenting symptoms in patients with malignant pleural effusion.

Figure (5). Percentage frequencies of physical signs in patients with malignant pleural effusion, other than signs of pleural effusion.

Figure (6). Correlations Matrix of biochemical profiles of pleural fluid in malignant patients

Figure (7). Histological type of malignant pleural effusion.

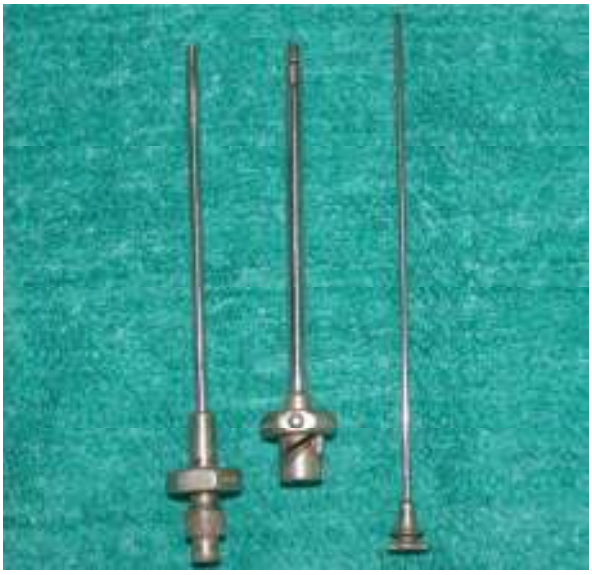


Figure 1: Abram's pleural biopsy needle

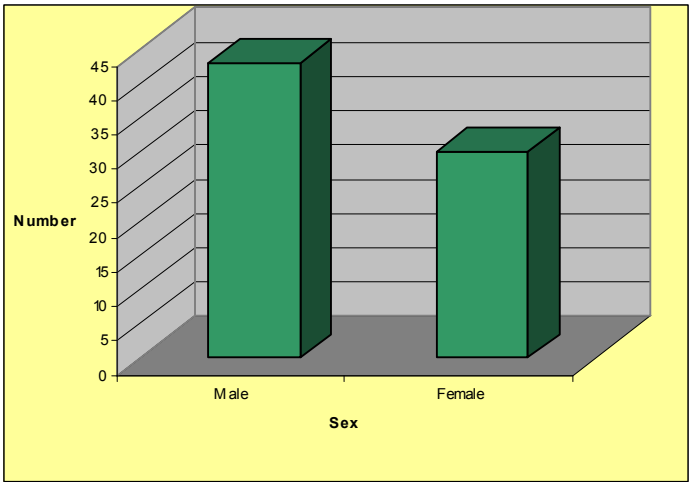


Figure 2: Sex distribution among patients with malignant pleural effusions.

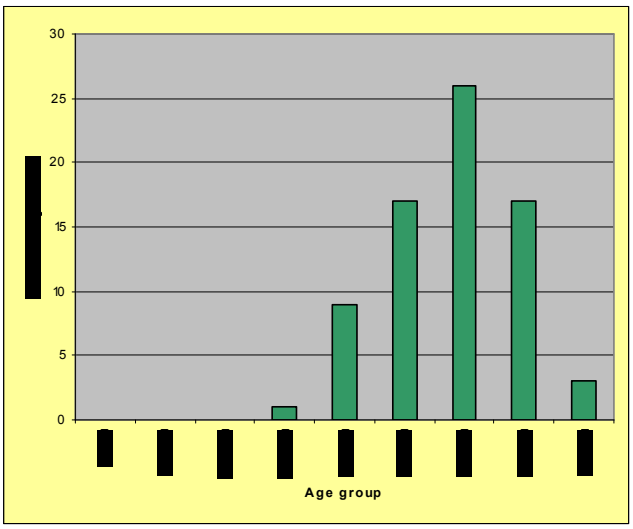


Figure 3: Histogram showing distribution of patients' age group in malignant pleural effusion

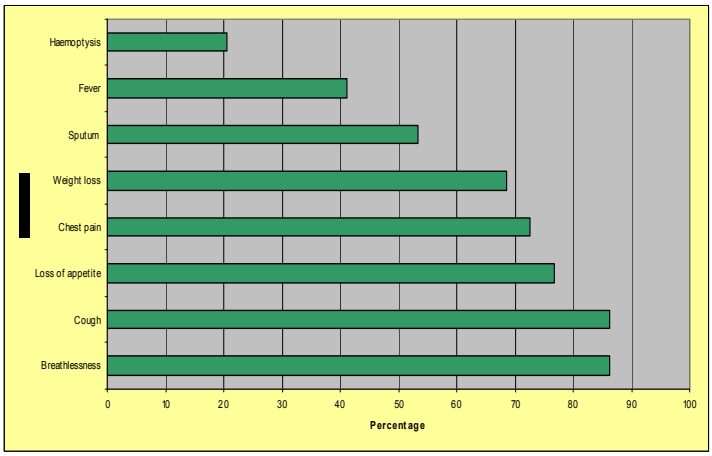


Figure 4: Percentage of presenting symptoms in patients with malignant pleural effusion.

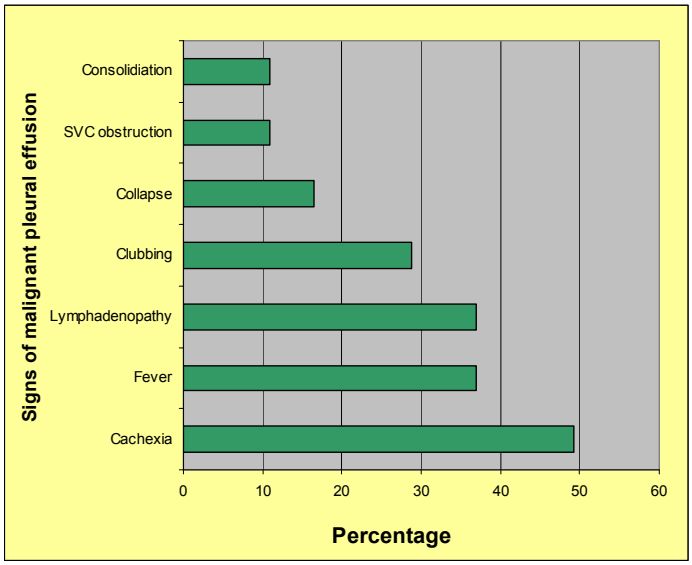
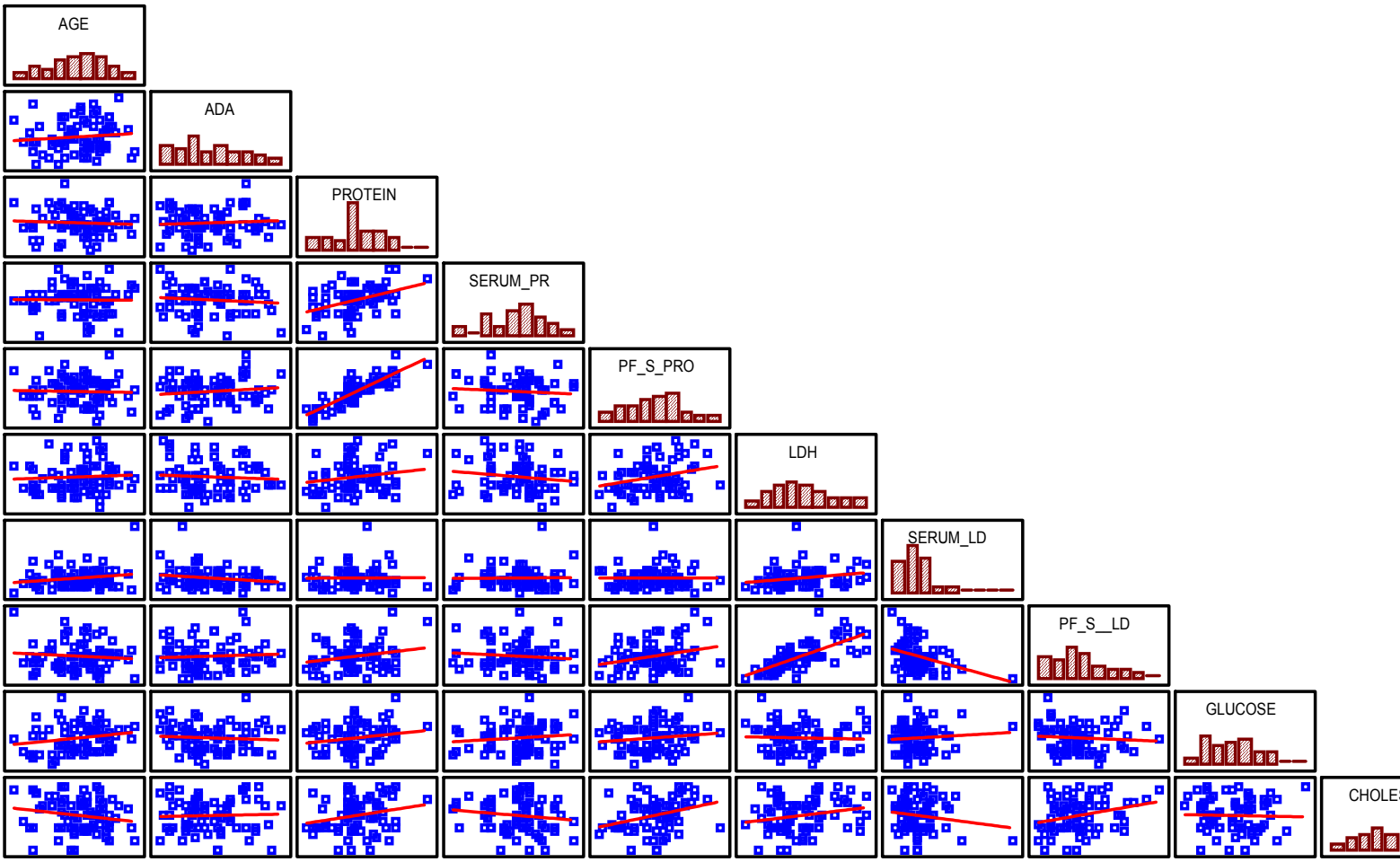


Figure 5: Percentage frequencies of physical signs in patients with malignant pleural effusion, other than signs of pleural effusion.

Figure 6: Correlations Matrix of biochemical profiles of pleural fluid in malignant patients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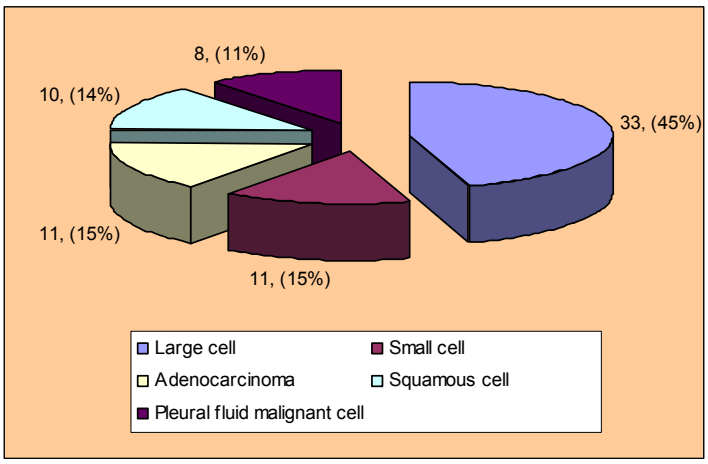

Figure 7: Histological type of malignant pleural effusion.